



## Cummulative Index 2004

### Volume 30

- February      IMMUNOLOGY FOR THE RHEUMATOLOGIST, pages 1–236  
May            NEW AND EMERGING THERAPIES FOR RHEUMATOID ARTHRITIS,  
                  pages 237–440  
August          APOPTOSIS IN THE RHEUMATIC DISEASES, pages 441–684  
November       OUTCOMES RESEARCH IN RHEUMATOLOGY, pages 685–921

Note: Page numbers of article titles are in **boldface** type.

### A

- A box domain, of HMGB1, for arthritis, 632  
Acetaminophen, for osteoarthritis, 705–706  
Adalimumab, for rheumatoid arthritis,  
    **347–362**  
    carcinogenic potential of, 360  
    disability effects of, 353–354  
    dosing of, 348  
    durability of response to, 355–356  
    early versus late, 356  
    efficacy of, 349  
    immunosuppressive effects of, 360  
    in breastfeeding, 360  
    in elderly persons, 359  
    in pregnancy, 359  
    methotrexate with, 349–350, 352,  
        355–357, 359  
    pharmacokinetics of, 347–348  
    pharmacology of, 347  
    precautions with, 359  
    quality of life impact of, 353–354  
    safety of, 242–252, 356–359  
    signs and symptom effects of, 349,  
        351–353  
    structural damage inhibition by, 354  
    tuberculosis risk from, 261–262

- Adenosine triphosphate, in apoptosis  
    regulation, 509

- Adhesion molecules, endothelial cell  
    interactions with, 99–103, 107–108

- Alcohol intake, uric acid levels and, 692

Alendronate, safety of, 842–843

American College of Rheumatology, data set  
    of, for rheumatoid arthritis assessment,  
        741–743

American Rheumatism Association  
    joint count system of, 726–728  
    Medical Information System of,  
        770–771, 880

Amyloid, serum, in apoptotic cell clearance,  
    476, 532

Anakinra, for rheumatoid arthritis, **363–378**  
    as monotherapy, 365–366, 369  
    efficacy of, 365–368  
    etanercept with, 316–317, 373–374  
    methotrexate with, 366–367, 369–370  
    multiple disease-modifying antirheumatic  
        drugs with, 370–372  
    previous tumor necrosis treatment with,  
        374–375  
    production of, 364–365  
    radiologic evaluation of, 289, 372–373  
    safety of, 242–252, 369–372  
    tuberculosis risk from, 256

Anaphylotoxin, complement-derived, 4–5

Anemia, aplastic, from cytokine inhibitors, for  
    rheumatoid arthritis, 247

Anergy

    B lymphocyte function in, 163  
    T lymphocyte function in, 151–152

- Angiogenesis  
endothelium role in  
    clinical perspectives of, 107–108  
    pathophysiology of, 104–107  
in rheumatoid arthritis, 44–45  
inhibitors of, 106–107
- Angioneurotic edema, hereditary, complement deficiencies in, 9
- Ankylosing spondylitis  
cytokines in, 46  
etanercept for, 320–321  
familial aggregation of, 214  
medical record data on, in Rochester Epidemiology Project, 821, 830
- Annexin I, lipoxin interactions with, 88
- Antibody(ies), high-mobility group box chromosomal protein 1, for arthritis, 632
- Anti-Fas, in apoptosis induction, 577–579
- Antigen-presenting cells  
B lymphocytes as, 168  
costimulatory molecule interaction with, 177–181  
in T-lymphocyte activation, 143–145  
T lymphocytes as, 136–138
- Antineutrophil cytoplasmic antibodies, in apoptosis, in kidney, 669
- Antinucleosome antibodies, in systemic lupus erythematosus, 537–546
- Antiphospholipid antibodies  
in apoptosis, 198  
treatment of, 11–12
- Antitumor Necrosis Factor Trial in Rheumatoid Arthritis with Concomitant Therapy (ATTRACT), 334–338, 704, 711
- Aplastic anemia, from cytokine inhibitors, for rheumatoid arthritis, 247
- Apoptosis, 193–212  
autoantigen structure alteration during, 455–471  
autoantigens in  
    biochemical alterations to, 197–198  
    description of, 193–195  
    redistribution during, 196  
    surface changes in, 198–199  
autoimmunity and, 557–572  
beneficial effects of, 507  
cells in  
    autoimmunity and, 204–206  
    auto-reactive T lymphocytes, 152  
    clearance of, 202–206  
    immune ignorance of, 202–203  
    peripheral tolerance of, 203–204  
    recognition of, 199–202
- clearance in, 473–485  
amyloid in, 476  
autoimmunity induction in, 474–475  
CD31 in, 479  
collectins in, 479  
complement in, 475–476, 481  
C-reactive protein in, 476  
DNA degradation in, 480  
environmental effects in, 480  
in systemic lupus erythematosus, 481–482, 495–499, 531–533  
manipulation of, for disease treatments, 482  
mannose-binding lectin in, 479  
Mer protein in, 477–478  
normal mechanisms in, 488–493  
phagocytosis triggers in, 474  
pharmacologic effects on, 480  
phosphatidylserine in, 476–477  
receptors in, 474, 479–481  
surfactant proteins in, 479  
transforming growth factor- $\beta$  in, 478  
transglutaminase 2 in, 478  
complement in, 7–8  
definition of, 507, 603  
essential nature of, 603  
in congenital heart block, 587–600  
in glomerulonephritis, 653–674  
in osteoarthritis, 637–651  
in rheumatoid arthritis, 601–623, 625–635  
in systemic lupus erythematosus. *See* Systemic lupus erythematosus, apoptosis in.  
mechanisms of, 441–454  
Bcl-2 family in, 446–451  
caspases in, 443–445  
DNases in, 445–446  
endoplasmic reticulum role in, 450–451  
extrinsic signaling through death receptors, 447–448, 488–491, 589–590  
intrinsic death pathways in, 448–450, 589–590  
phagocytosis after, 25  
resistance to, in rheumatoid arthritis, therapy based on, 607–617  
T-cell receptor signaling and, 145–146  
Toll-like receptor stimulation and, 557–572  
versus necrosis, 638
- Apoptosis-inducing factor/endonuclease G, 445
- Apoptosomes, 448

- Arachidonic acid, lipoxin formation from, 71–75
- Arteritis, giant cell, 54–55, 821, 825
- Arthritis
- carcinomatous, versus rheumatoid arthritis, 276–277
  - collagen-induced, treatment of, 12
  - degenerative. *See* Osteoarthritis.
  - high-mobility group box chromosomal protein 1 in, 630–632
  - in cancer, versus rheumatoid arthritis, 279–281
  - in paraneoplastic syndromes, versus rheumatoid arthritis, 276–279
  - psoriatic. *See* Psoriatic arthritis.
  - reactive, cytokines in, 46
  - rheumatoid. *See* Rheumatoid arthritis.
- Arthritis, Rheumatism and Aging Medical Information System (American Rheumatism Association Medical Information System), 770–771, 880
- Arthritis Impact Measurement Scale, 730, 737, 883–884
- Aspartic acid-specific apoptotic proteases, in autoantigen cleavage, 460–461
- Aspirin, safety of, 839, 841  
in pregnancy, 842
- Aspirin-triggered lipoxins
- actions of, 73–75, 79–81
  - agonists of, 75
  - formation of, in disease, 78
  - in proinflammatory gene expression, 86–87
  - overview of, 68–71
  - receptors for, 83–87
  - therapies related to, 87–90
- ATTRACT (Antitumor Necrosis Factor Trial in RA with Concomitant Therapy), 334–338, 704, 711
- Auranofin, for rheumatoid arthritis, 713
- Autacoids, in inflammation resolution. *See* Inflammation, resolution of, endogenous small molecules for.
- Autoantigens
- distribution of, autoimmune disease nature and, 220–221
  - in apoptosis
  - biochemical alterations to, 197–198
  - description of, 193–195
  - redistribution during, 196
  - structural alterations in, 455–471
  - aspartic acid-specific protease cleavage in, 460–461
  - crypticity in, 456–460
- cytotoxic lymphocyte granule-induced death and, 461–464
- dominance in, 456–458
- granzyme B-induced cleavage in, 464, 533
- phenotype-specific, 464–465
- posttranslational, 465–466, 533
- tolerance induction in, 456
- surface changes in, 198–199
- Autodigestion, in apoptosis, in osteoarthritis, 646
- Autoimmune disease
- apoptosis dysregulation in, 204–206
  - B lymphocytes in, 167–168
  - classification of, versus major histocompatibility class, 221–222
  - complement and, 7–9, 11–13
  - dendritic cell cross-priming in, 125–127
  - genetics of, 213–227
  - familial aggregation, 213–215
  - low penetrance rates, 215–216
  - major histocompatibility genes in, 216–224
  - allele association in, 222–224
  - disease classification based on, 221–222
  - importance of, 217–218
  - physiologic response and, 218–220
  - target autoantigen distribution and, 220–221
  - T-lymphocyte repertoire in, 224–227
  - twin concordance, 215
- in rheumatoid arthritis therapy, 249–251, 340–341
- T lymphocytes in, 149–153
- treatment of, B lymphocyte considerations in, 169–170
- Autoimmunity
- DNase and, 480
  - in apoptosis, 474–475
  - antigen structural alterations in, 455–471
  - in clearance alterations, 497–499
  - Toll-like receptors and, 557–572
- Autophagy, in apoptosis, in osteoarthritis, 645–646
- Azathioprine, safety of, in pregnancy, 841
- 
- B**
- B23 autoantigen, structural alterations of, in apoptosis, 464–465
- B lymphocytes, 159–174
- activation of, 164–165
  - regulation of, 165–167

- anergic, 163  
as antigen-presenting cells, 177  
autoimmunity and, 49–50, 167–170  
depletion of, for rheumatoid arthritis  
treatment, 391–401  
aim of, 391–393  
immunodynamic studies of,  
399–400  
immunosuppression evidence in,  
396–397  
infusion reactions from, 397–398  
justification for, 396  
length of benefit of, 396  
malignancy in, 398  
mechanics of, 393–394  
practical experience with, 394  
protocols for, 394–395  
seronegative, resistance of, 395  
follicular, 165  
immunoglobulins produced by, 160–162  
in systemic lupus erythematosus development, 498, 516–517, 519–521  
marginal zone, 164–165  
memory, 165  
rheumatoid factor produced by,  
chromatin-containing immune complexes in, 560–564  
selection of, 163–164  
subsets of, 164–165  
therapeutics and, 169–170  
tolerance in, 162–164
- B7 molecules, action of, 177–178, 181–182
- Bacterial DNA, immunogenic effects of, 558
- Bad protein, in apoptosis, 447, 450
- Bak proteins, in apoptosis, 446–451, 603
- Bax proteins, in apoptosis, 446–451, 603
- B-cell activating factor  
in B-lymphocyte activation, 166–167  
in systemic lupus erythematosus, 50
- B-cell receptor and B-cell receptor complex, 136, 163–166
- B-cell stimulatory/differentiating factor. *See* Interleukin-6.
- Bcl-2 proteins, in apoptosis, 446–451  
in rheumatoid arthritis, 602–603,  
615–616  
in systemic lupus erythematosus, 529
- B-E8 monoclonal antibody, for rheumatoid arthritis, 408–410
- Behcet's disease, cytokines in, 56
- BH3-only proteins, in apoptosis, 447,  
449–450
- Bias  
in pharmacoepidemiology, 837–838  
minimization of, in Rochester Epidemiology Project, 827–829
- Bid protein, in apoptosis, 447  
autoantigen structural alterations and, 462  
in rheumatoid arthritis, 603
- Bim protein, in apoptosis, 447, 450
- Binding proteins, interleukin-18, 421–424
- Black Women's Health Study, 800, 807
- Bleeding, gastrointestinal,  
NSAID-induced, 839
- Blood vessels, endothelium of. *See* Endothelial cells, vascular
- Bok proteins, in apoptosis, 446–450
- Bone marrow, apoptotic cell clearance in, 360
- Bone mineral density reference values, in NHANES, 875
- Breast implants, rheumatic disease in,  
prospective cohort studies on, 803–804
- Breastfeeding, adalimumab use in, 360
- Button test, in rheumatoid arthritis assessment, 738
- 
- C
- C1 inhibitor, action of, 5
- Cachexia, cardiac, from cytokine inhibitors, for rheumatoid arthritis, 253
- CAD/DFF40, in apoptosis, 445
- Cadherins, in phagocytosis, 22
- Cancer, 271–284  
from antirheumatic drug therapy,  
248–249, 274–276  
adalimumab, 358, 360  
etanercept, 323  
infliximab, 341–342  
rituximab, 398  
in rheumatoid arthritis, 858–859  
mimicking rheumatoid arthritis,  
279–281  
paraneoplastic syndromes due to, versus rheumatoid arthritis, 276–279  
risk of, in rheumatoid arthritis, 271–274
- Cancer Registry, of Scandinavian countries, 854, 858–859, 862
- Carcinomatous polyarthritis, versus rheumatoid arthritis, 276–277

- Cardiac cachexia, from cytokine inhibitors, for rheumatoid arthritis, 253
- Cartilage, destruction of. *See* Osteoarthritis.
- Case reports, in observational research, 685–686, 691
- Case-control surveillance methodology  
causal inferences from, 692–696  
for pharmacoepidemiology, 837
- Caspase(s), in apoptosis, 443–445  
autoantigen structural alterations  
and, 461  
in rheumatoid arthritis, 601–602
- Caspase inhibitors  
for apoptotic cell clearance, 482, 647  
for glomerulonephritis, 670  
for osteoarthritis, 647
- Caspase-activated DNase, in apoptosis, 445
- Cathepsins, in apoptosis, in osteoarthritis, 645
- Causal inference, principles of, 686–691  
causal (structural) models, 691  
conventional methods, 689–690  
conventional modeling, 690–691  
definitions in, 686–687  
inverse probability of treatment  
weighting methods, 690  
observational studies, 688–689  
randomized trials, 687–688
- Causation, definition of, 686–687
- Cause of Death Registry, of Scandinavian countries, 854, 857–858
- CD14 dendritic cells, 116–118
- CD28  
in B-lymphocyte activation, 167  
in T-lymphocyte afferent signal regulation, 179–182, 186
- CD31, in apoptotic cell clearance, 479
- CD34 dendritic cells, 116–117
- CD40 and C40 ligand  
in B-lymphocyte activation, 167  
in systemic lupus erythematosus, 49–50  
in T-lymphocyte efferent signal regulation, 182–186
- CD59  
deficiency of, autoimmune disease in, 9  
in complement activation, 6
- CD64 antibody, toxin to, in fusion protein, for rheumatoid arthritis, 611–612
- CD69 tingible body macrophages, in systemic lupus erythematosus, 519–520
- CD91, in apoptotic cell clearance, 479
- cdc42, in apoptotic cell clearance, 474
- Celecoxib  
for osteoarthritis, 705–706  
safety of, 840–841
- Cells  
necrosis of. *See* Necrosis.  
programmed death of. *See* Apoptosis.
- CENP-C (scleroderma autoantigen), cleavage of, in apoptosis, 463
- Central Finland Rheumatoid Arthritis Database, 775
- Centrocytes, apoptosis of, 518–519
- Channeling, of drugs, 845
- Chemokines  
in angiogenesis, 105–106  
in phagocytosis, 21, 27–29
- Chemotherapy, rheumatism due to, versus rheumatoid arthritis, 276, 278–279
- Chondrocytes, apoptosis of (chondroptosis), 640, 644–646. *See also* Osteoarthritis, apoptosis in.
- Chromatin  
fundamental unit of. *See* Nucleosomes.  
in immune complexes, Toll-like receptors and, 560–564
- Citrullination, in apoptosis, in autoantigen structural alterations, 466
- Clinical trials and clinical care  
for data collection, 761, 763–764  
rheumatoid arthritis assessment in, 725–751
- Clodronate, apoptotic cell clearance and, 480
- Clonal ignorance, T lymphocyte function in, 151–152
- Cohort studies, prospective. *See* Prospective cohort studies.
- Collagen IV, as apoptosis protection, 660
- Collagen-induced arthritis, treatment of, 12
- Collectins, in apoptotic cell clearance, 479, 594
- Colorectal cancer, in rheumatoid arthritis, 272–273
- Comparability, in observational research, 686–687, 689–690
- Complement, 1–18  
activation of, 1–3  
autoimmunity and, 7–9, 11–13  
deficiencies of, 7–9

- dual roles of, 12  
effector functions of, 3–5  
in apoptosis, 198–202, 475–476,  
481, 488  
in systemic lupus erythematosus,  
496, 517–518  
receptors for  
deficiencies of, 9–11  
on phagocytes, 24  
regulation of, 5–6
- Concordance, twin, in autoimmune disease, 215
- Confidentiality, of patient information, in Rochester Epidemiology Project, 831
- Confounding factors  
in pharmacoepidemiology, 837–838  
in Rochester Epidemiology Project, 826
- Congenital heart block, **587–600**  
apoptosis in  
consequences of, 594–598  
in vitro evidence of, 589–591  
in vivo evidence of, 591–594  
versus physiologic apoptosis,  
588–589  
differential diagnosis of, 588
- Congestive heart failure, infliximab for, 342
- Connective tissue disorders, prospective cohort studies on, 800, 804
- Consortium of Rheumatology Researchers of North America, 880
- Corticosteroids  
for glomerulonephritis, 669  
for rheumatoid arthritis, tuberculosis risk from, 260–261  
resolvins and, 87–90  
safety of, in pregnancy, 842
- Cost analysis, 889
- Cost benefit studies, 888
- Cost effectiveness studies, 887–888
- Cost minimization studies, 887–888
- Cost utility studies, 888
- Costimulatory molecules, **175–191**. *See also specific molecules.*  
B-lymphocyte activation by, 166  
description of, 175–176  
families of, 176  
T-lymphocyte interactions with  
afferent signals, 178–182  
animal studies of, 184–185  
efferent signals, 182–184  
in rheumatic diseases, 185  
therapeutic applications of, 185–187  
two-signal model of, 177–178
- Cost-of-illness studies, in Rochester Epidemiology Project, 830
- Counterfactual process, in observational research, 687
- CpG DNA, in apoptosis induction, 577–579
- C-reactive protein  
in apoptosis regulation, 476, 510–511,  
517  
in rheumatoid arthritis assessment, 726,  
729–730
- Crithidia luciliae immunofluorescent test, for autoantibodies, drug-induced, 340
- CrmA protein, in apoptosis, 444
- Cross-over design  
in observational research, 696  
in rheumatoid arthritis clinical trials,  
705–706
- Cross-sectional studies, in observational research, 691–692
- Crry-immunoglobulin, for autoimmune disease, 11
- Crypticity, in apoptosis, 456–460
- Cyclooxygenase inhibitors, for apoptotic cell clearance, in osteoarthritis, 647–648
- Cyclooxygenase-1 inhibitors, economic evaluation of, 890
- Cyclooxygenase-2 inhibitors  
channeling of, 845  
safety of, 840–841
- Cyclophosphamide, for rheumatoid arthritis, rituximab with, 394–395
- Cyclosporine, for rheumatoid arthritis, methotrexate with, 704
- Cytochrome c, in apoptosis, in rheumatoid arthritis, 602
- Cytokines, **39–65**. *See also specific cytokines.*  
complement modification of, 8  
in angiogenesis, 105  
in apoptosis, 535–536, 660–661  
in Behcet's disease, 56  
in giant cell arteritis, 54–55  
in inflammatory myopathies, 53–54  
in juvenile rheumatoid arthritis, 46–47  
in osteoarthritis, 47  
in phagocytosis, 27–29  
in rheumatoid arthritis, 40–46  
in spondyloarthropathies, 46  
in systemic lupus erythematosus, 47–52  
in systemic sclerosis, 52–53  
in T-cell receptor signaling, 145  
in tuberculosis, 259–260

- in vasculitis, 54–56  
in Wegener's granulomatosis, 55–56
- Cytotoxic T lymphocyte(s), 148–149
- Cytotoxic T lymphocyte antigen 4, in  
T-lymphocyte afferent signal regulation,  
179–182, 186
- Cytotoxic T-lymphocyte antigen  
4-immunoglobulin, for rheumatoid  
arthritis, 379–389  
autoimmune disease and, 379–381  
clinical studies of, 383–385  
mechanism of action of, 385–387  
methotrexate with, 383–385  
preclinical studies of, 382–383  
source of, 382  
structure of, 381–382
- D**
- Danger model, of immune response, 151
- Databases  
American Rheumatism Association  
Medical Information System,  
770–771, 880  
Central Finland Rheumatoid Arthritis  
Database, 775  
Consortium of Rheumatology  
Researchers of North America, 880  
German Regional Collaborative Arthritis  
Centers, 774–775  
ideal, 883  
Italian, 777  
Nashville, Tennessee, 772–773  
National Data Bank for Rheumatic  
Diseases, 753–768  
National Health and Nutrition Examina-  
tion Surveys (NHANES), 869–878  
Oslo Rheumatoid Arthritis Registry,  
773–774  
pharmacoepidemiology, 836–837  
problems with, 879–883  
rheumatoid arthritis, 769–781  
Rochester Epidemiology Project,  
819–834  
Scandinavian, 851–867  
Spanish, 776–777  
Standard Diagnosis Registry of  
Rheumatic Diseases, 773  
Swedish registry of biologic agents and  
leflunomide, 776  
uniform, 777  
Wichita Database and National Data  
Bank, 771–772
- Death effector domains, in apoptosis, 443, 601
- Death receptor pathway, for apoptosis, in  
rheumatoid arthritis, 601
- Death-associated molecular patterns (DAMPs),  
in apoptosis, 490–491, 493–494
- Death-inducing signaling complex, in  
apoptosis, 445, 447–448
- Decay accelerating factor  
action of, 5–6  
deficiency of, autoimmune disease in,  
9–10
- Deimination, in apoptosis, in autoantigen  
structural alterations, 466
- Demyelinating disorders, from rheumatoid  
arthritis therapy  
cytokine inhibitors, 247  
etanercept, 322–323
- Dendritic cells, 115–134  
cross-priming by, 125–127  
historical overview of, 115–116  
immune complex interactions with,  
Toll-like receptors and, 564  
immunogenic, 121–123  
in apoptosis, 203–204, 473,  
491–493, 520  
interleukin-18 production from, 419  
maturation of, 121–123, 509, 630  
monocyte-derived  
development and function of,  
116–118  
in rheumatoid arthritis, 123–127  
myeloid  
development and function of,  
116–118  
early control of, 118–119  
ontogeny of, 116  
plasmacytoid, 119–120  
receptors on, 120–123  
subtypes of, 116  
tolerogenic, 123–124, 152–153
- Dermatomyositis, cytokines in, 53–54
- Descriptive observational research, 685–686
- Dexamethasone, in apoptosis induction,  
577–579
- Diabetes mellitus, autoimmune, dendritic cell  
cross-priming in, 125–126
- Diagnostic criteria, in Rochester Epidemiology  
Project, 821
- Diagnostic tests, observational studies for, 696
- Diapedesis, in phagocytosis, 21–22
- Diclofenac, for osteoarthritis, 705
- Dihydroorotate dehydrogenase, leflunomide  
inhibition of, 293–294

- Disability  
databases on, 860  
in elderly, in NHANES, 873–874
- Disease activity score, for rheumatoid arthritis  
assessment, 742–743
- Disease-modifying antirheumatic drug therapy.  
*See also specific drugs.*  
anakinra with, 370–372  
economic evaluation of, 888–891  
for inflammatory polyarthritis, 694  
malignancy due to, 274–276
- DNA  
antibodies to, in systemic lupus erythematosus, 516–517  
bacterial, immunogenic effects of, 558  
degradation of, in apoptotic cell clearance, 480, 603–604  
release of, in systemic lupus erythematosus, 573–585  
agents inducing, 577–579  
assays for, 576–577  
cell death processes and, 574–575  
in dead and dying cell administration, 579–582  
properties of, 575–576
- DNases, in apoptosis, 445–446, 480, 518, 532
- Docosahexaenoic acid, resolvins synthesized from, 90
- Dominance, immunologic, in apoptosis, 456–458
- Drugs  
economic evaluation of, 888–891  
research on. *See Pharmacoepidemiology.*
- dsDNA, antibodies to, in systemic lupus erythematosus, 516–517
- E**
- Economic aspects, of health services research, 887–889
- Eicosanoid oxidoreductase, inhibition of, 76
- Elderly persons  
adalimumab therapy in, 359  
disability in, in NHANES, 873–874
- Encounter-specific data, in Rochester Epidemiology Project, 821
- Endoplasmic reticulum, in apoptosis, 450–451
- Endothelial cells, vascular, 97–114  
adhesion molecule interactions with, 99–103, 107–108  
apoptosis of, in glomerulonephritis, 662–663
- cytokine production in, in rheumatoid arthritis, 42–44  
in angiogenesis, 104–108  
in inflammation, 98–99, 103  
lipoxin effects on, 83  
morphology of, 98–99  
permeability of, 98–99
- Endotoxemia, high-mobility group box chromosomal protein 1 (HMGB1) in, 627
- Enterocytes, lipoxin effects on, 81
- Eosinophilic fasciitis, versus rheumatoid arthritis, 276, 278
- Epidemiologic research  
databases for. *See Databases.*  
observational studies in. *See Observational research.*
- Epidemiologic studies  
of osteoarthritis, 783–797  
pharmacoepidemiology, 835–850  
Rochester Epidemiology Project, 819–834
- Epithelial cells  
apoptosis of, in glomerulonephritis, 662  
aspirin-triggered lipoxin effects on, 86–87
- Epitope spreading, B lymphocytes in, 168
- Erythrocyte sedimentation rate, in rheumatoid arthritis assessment, 726, 729–730
- Esophageal cancer, in rheumatoid arthritis, 272–273
- Etanercept  
for ankylosing spondylitis, 320–321  
for juvenile chronic arthritis, 317–318  
for psoriatic arthritis, 318–320  
for rheumatoid arthritis, 309–326, 703  
absorption of, 310  
anakinra with, 316–317, 373–374  
early, 315–316  
economic evaluation of, 890  
methotrexate with, 313–314, 316  
once weekly dosage for, 317  
pharmacokinetics of, 310  
pharmacology of, 309–310  
phase II studies of, 310–311  
phase III studies of, 311–312  
radiologic evaluation of, 289–290, 315–316  
safety of, 242–252  
structure of, 309  
toxicity of, 322–323  
tuberculosis risk from, 261–262  
versus methotrexate, 314–316, 711  
for Wegener's granulomatosis, 321
- Etoposide, for rheumatoid arthritis, 611

- Evidence-based rheumatology  
 clinical trials in, 701–724  
 data collection, maintenance, and analysis for, 753–768  
 health services research in, 879–898  
 national databases in, 851–867, 869–878  
 National Health and Nutrition Examination Surveys (NHANES), 869–878  
 observational research in, 685–699  
 osteoarthritis epidemiologic studies in, 783–797  
 pharmacoepidemiology in, 835–850  
 prospective cohort studies in, for risk factor determination, 799–817  
 rheumatoid arthritis databases in, 769–781  
 rheumatoid arthritis quantitative measures and indices in, 725–751  
 Rochester Epidemiology Project in, 819–834
- Extracellular matrix  
 as apoptosis protection, 660  
 phagocytic activity in, 22
- Eye, lipoxin effects on, 83
- 
- F**
- Factor H  
 action of, 5–6  
 deficiency of, autoimmune disease in, 10
- FADD protein, in apoptosis, 447, 462  
 in congenital heart block, 589–590, 593  
 in rheumatoid arthritis, 601
- Familial aggregation, of autoimmune disease, 213–215
- Farming exposure, systemic vasculitis and, 693
- Fas and FasL, in apoptosis, 447–448, 491, 660–661  
 in autoantigen structural alterations, 461–462  
 in congenital heart block, 589–590, 593  
 in rheumatoid arthritis, 601, 609–610, 612–613  
 in systemic lupus erythematosus, 529
- Fasciitis, palmar, versus rheumatoid arthritis, 276, 278
- Fasciitis-panniculitis syndrome, versus rheumatoid arthritis, 276, 278
- Fatigue measurement, for rheumatoid arthritis assessment, 737
- FcgR receptors  
 in phagocytosis, 23–24  
 in T-lymphocyte afferent signal regulation, 179–180
- FcgRIIA, in apoptosis, in systemic lupus erythematosus, 518
- Fetus, heart block in. *See* Congenital heart block.
- Fibroblasts  
 in apoptosis, in rheumatoid arthritis, 612–616  
 lipoxin effects on, 81, 87
- FLICE-like inhibitory protein family (FLIP), in apoptosis, 444–445, 448  
 in rheumatoid arthritis, 601, 609–610, 612–613
- Framingham Study, 801, 812–814
- Functional evaluation, for rheumatoid arthritis assessment, 726, 738–739
- 
- G**
- Gastrointestinal system  
 alendronate effects on, 842–843  
 inflammation of, lipoxin in, 82  
 NSAID effects on, 839
- GATA-3 transcription factor, T lymphocytes and, 146
- Genealogy Database, of Scandinavian countries, 855–856, 859–860
- Genetic factors  
 in autoimmune disease. *See* Autoimmune disease, genetics of.  
 in rheumatoid arthritis, 859–860  
 in Rochester Epidemiology Project, 825–826  
 in systemic lupus erythematosus, 517–518
- German Regional Collaborative Arthritis Centers, 774–775
- Germinal centers, of lymph tissue, apoptotic cell clearance in, 512, 518–521
- Giant cell arteritis  
 cytokines in, 54–55  
 medical record data on, in Rochester Epidemiology Project, 821, 825
- Global measures, for rheumatoid arthritis assessment, 726, 738–739
- Glomerulonephritis, apoptosis in, 653–674  
 antineutrophil antibodies in, 543–546  
 cell recognition and phagocytosis in, 654–655  
 detection of, 656–658  
 incidence of, 655  
 kinetics of, 654  
 mechanisms of, 658–661, 667–669

- modulation of, 669–670  
of endothelial cells, 662–663  
of epithelial cells, 662  
of leukocytes, 664–667  
of mesangial cells, 658–661  
tubulointerstitial, 663–664
- Glucocorticoid-induced leucine zipper protein, in phagocytosis, 33
- Gold salts, for rheumatoid arthritis, 709, 713
- Gout  
medical record data on, in Rochester Epidemiology Project, 821  
prospective cohort studies on, 801, 809–812
- Granules, in neutrophils, in phagocytosis, 26–27
- Granulocytes, impaired activity of, in systemic lupus erythematosus, 514–515
- Granzymes  
in apoptosis, 198, 462–464, 533  
in cytotoxic T lymphocytes, 148
- Grip strength, in rheumatoid arthritis assessment, 738
- Growth factors, in angiogenesis, 104–105
- Gruppo Italiano Artrite Reumatoide Aggressiva database, 777
- GULP protein, in apoptotic cell clearance, 474
- 
- H**
- Hand, osteoarthritis of, prospective cohort studies on, 813
- Health Assessment Questionnaire, 730–735, 883–884
- Health Insurance Portability and Accountability Act, 831
- Health Professionals Follow-up Study, 801, 808–810
- Health services research, 879–898  
databases for, problems with, 879–883  
economic aspects of, 887–889  
instruments for  
disease-specific, 883–884  
generic, 883–886  
selection of, 884–885  
theoretical construct of, 884  
on new treatments, 889–891  
patient self-assessment in, 886
- Heart, apoptosis in, 588–589
- Heart block, congenital. *See* Congenital heart block.
- Heart failure  
from cytokine inhibitors, for rheumatoid arthritis, 253  
infliximab for, 342
- Helper T lymphocytes, 146–148
- Hemoglobinuria, paroxysmal nocturnal, complement deficiency in, 9–10
- Hemolytic uremic syndrome, in factor H defects, 10
- Hepatocellular carcinoma autoantigen, structural alterations of, in apoptosis, 464–465
- Hereditary angioneurotic edema, complement deficiencies in, 9
- High endothelial venule-like microvessels, in inflammation, 99–100
- High-affinity ligand binding, in apoptosis, autoimmunity induction in, 459–460
- High-mobility group box chromosomal protein 1 (HMGB1), 625–635  
biochemistry of, 628–629  
discovery of, 626  
extracellular release of, 629–630  
in arthritis, 630–632  
in necrosis, 509  
in severe sepsis, 627–628  
inhibitors of, for arthritis, 632  
receptors for, 628
- Hip  
fractures of, prospective cohort studies on, 813–814  
osteoarthritis of, prospective cohort studies on, 804–805
- Histamine-mediated injury, to endothelial cells, 98
- Histones, in apoptosis, 534
- Histoplasmosis, risk of, in etanercept therapy, 322
- HLAs. *See* Human leukocyte antigens.
- HMGB1. *See* High-mobility group box chromosomal protein 1 (HMGB1).
- Hospital Discharge Registry, of Scandinavian countries, 855, 858–859, 861
- Hrd1, in apoptosis, in rheumatoid arthritis, 615
- Human immunodeficiency virus infection  
HLAs in, 222–223  
incompetent cytotoxic T lymphocytes in, 149
- Human leukocyte antigens, in autoimmune disease, 216–224  
allele association in, 222–224

- disease classification based on, 221–222  
importance of, 217–218  
physiologic response and, 218–220  
target autoantigen distribution and,  
220–221  
T-lymphocyte repertoire in, 224–227
- Human subjects, protection of, in Rochester Epidemiology Project, 831
- Hyaluronan, for osteoarthritis, 648
- Hydroxychloroquine, for rheumatoid arthritis, 703, 705, 709
- 15-Hydroxyprostaglandin dehydrogenase, inhibition of, 76
- Hypocomplementemia, in pregnancy, 10
- 
- I
- Ibuprofen, safety of, 839  
in pregnancy, 842
- Immune complexes, chromatin-containing, Toll-like receptors and, 560–564
- Immune ignorance, in apoptosis, 202–203
- Immune thrombocytopenia, rituximab for, 398
- Immunity, innate, T lymphocytes and, 141–143
- Immunoglobulin(s)  
cytotoxic T-lymphocyte antigen 4, for rheumatoid arthritis, 379–389  
description of, 160–162
- Immunoglobulin G, in congenital heart block, 593–594
- Immunoglobulin M, in apoptotic cell clearance, 532
- Immunoglobulin superfamily  
costimulatory function of, 176  
in leukocyte-endothelial interactions, 101
- Immunoglobulin-like transcript-like receptors, of dendritic cells, 120
- Immunologic synapse, in T-lymphocyte activation, 143–145
- Immunology  
apoptosis. *See* Apoptosis.  
complement. *See* Complement.  
costimulatory molecules, 166, 175–191  
cytokines. *See* Cytokines.  
dendritic cells. *See* Dendritic cells.  
endogenous small molecules for  
inflammation resolution, 67–95  
endothelial cells, 42–44, 97–114  
genetic factors in, 213–227
- lymphocytes. *See* B lymphocytes;  
T lymphocytes.  
phagocytes, 19–38, 199–200
- Immunoreceptor tyrosine-based activation motifs, in B-lymphocyte activation, 166
- Inactivity, in NHANES, 874
- Inclusion body myositis, cytokines in, 53–54
- Inducible costimulator molecule, 179, 182, 186
- Infections  
from rheumatoid arthritis therapy  
adalimumab, 357–358  
cytokine inhibitors, 243–247  
infliximab, 339–340  
lipoxin in, 82
- Inflammation  
endothelial cells and  
adhesion regulation in, 103  
morphology and permeability of, 98–99  
in systemic lupus erythematosus, 52  
in T-lymphocyte dysregulation, 146–147  
interleukin-6 in, 406–407  
interleukin-18 in, 420  
phagocytes. *See* Phagocytes.  
resolution of, endogenous small molecules for, 67–95  
agonists, 75–77  
cell-cell interaction in, 71–75  
disease associations of, 77–83  
in combination therapies, 87–90  
new, 90–91  
overview of, 67–71  
receptors for, 83–87  
resolvins, 90–91  
types of, 68  
treatment of, angiogenesis inhibitors in, 108
- Inflammatory bowel disease  
cytokines in, 46  
interleukin-18 in, 426–427
- Inflammatory myopathies, cytokines in, 53–54
- Inflammatory polyarthritis, disease-modifying antirheumatic drug therapy for, 694
- Infliximab  
economic evaluation of, 890  
for congestive heart failure, 342  
for rheumatoid arthritis, 327–345  
apoptosis induction in, 606–607  
in early disease, 337–339  
methotrexate with, 332–338  
pharmacokinetics of, 333  
phase II trials of, 330–334  
phase III trials (ATTRACT) of, 334–338

- proof of principle trials of, 327–330  
radiologic evaluation of, 289–291  
safety of, 242–252, 339–342  
single-infusion, 330–332  
tuberculosis risk from, 261–264
- Infusion reactions, from cytokine inhibitors, for rheumatoid arthritis, 243
- Inhibitors of apoptosis proteins, 443–444
- Injection site reactions, from cytokine inhibitors, for rheumatoid arthritis, 242
- Insulin-like growth factor 1, for glomerulonephritis, 670
- Integrins  
in angiogenesis, 106  
in leukocyte-endothelial interactions, 100  
in phagocytosis, 21–22
- Intercellular cell adhesion molecule-1, in leukocyte-endothelial interactions, 101
- Intercellular gaps, in endothelium, 98–99
- Interferon- $\beta$ , for apoptotic cell clearance, 482
- Interferon- $\gamma$   
in interleukin-18 binding protein expression, 423  
in phagocytosis, 31  
interleukin-18 production and, 415–416, 420
- Interleukin(s)  
in angiogenesis, 105  
in inflammatory myopathies, 53–54  
in leukocyte-endothelial interactions, 103  
in osteoarthritis, 47  
in phagocytosis, 21–22, 25, 30–35  
in rheumatoid arthritis, 41–45  
in systemic lupus erythematosus, 50–52
- Interleukin-1  
family of, 415  
in apoptosis, in osteoarthritis, 643
- Interleukin-1 receptor antagonists, anakinra as.  
*See* Anakinra.
- Interleukin-18, secretion of, 418
- Interleukin-18 converting enzyme (ICE, caspase-1)  
in interleukin-18 production, 416  
interleukin-18 processing without, 419–420
- Interleukin-6, 403–413  
function of, 406  
in apoptosis, in rheumatoid arthritis, 616  
in rheumatoid arthritis pathogenesis, 406–407
- inhibitors of, for rheumatoid arthritis, 407–410  
receptor for, in signal transduction, 405  
structure of, 404–405  
superfamily of, 404–405  
synonyms for, 404
- Interleukin-15, in rheumatoid arthritis, 607
- Interleukin-18  
in hepatic injury, models of, 427–428  
in inflammatory bowel disease, models of, 426–427  
in rheumatoid arthritis pathogenesis, 415–432  
historical review of, 415–416  
mechanisms of, 416–417, 420  
models of, 424–426  
processing of, 419–420  
production of, 417–420  
protein binding and, 421–424  
P2X-7 receptor and, 418–419  
release of, 417–420  
soluble receptor of, 423–424
- Internet, outcomes questionnaires on, 759, 761–762
- Inverse probability of treatment weighting methods, in observational research, 690
- Iowa Women's Study, 800, 805–807
- Isoaspartyl linkages, in apoptosis, in autoantigen structural alterations, 465–466
- 
- J**
- Janus kinase, in phagocytosis, 34–35
- Johns Hopkins Precursor Study, 801, 811–812
- Joint counts, for rheumatoid arthritis assessment, 726–728, 739
- Juvenile chronic arthritis/juvenile rheumatoid arthritis  
cytokines in, 46–47  
etanercept for, 317–318  
interleukin-6 monoclonal antibody for, 410  
medical record data on, in Rochester Epidemiology Project, 821, 825
- 
- K**
- Kidney  
apoptosis in  
beneficial aspects of, 655–656  
cell recognition and phagocytosis in, 654–655  
defective, 667–669  
deleterious, 655. *See also* Glomerulonephritis.

- detection of, 656–658  
in inflammation, 656–658  
kinetics of, 654  
modulation of, 669–670  
of endothelial cells, 662–663  
of glomerular epithelial cells, 662  
of leukocytes, 664–667  
of mesangial cells, 658–661  
stimulation of, 660–661  
failure of, NSAID-induced, 840  
inflammation of, lipoxin in, 82
- Knee, osteoarthritis of  
epidemiology of, 783–784  
prospective cohort studies on, 794–795,  
811–813  
preparing for, 789–794  
radiology of, 787–788  
risk factors for, 788–789
- L**
- Laboratory tests, for rheumatoid arthritis  
assessment, 726, 729–730, 739
- Lucunae, cell remnant extrusion into, in  
apoptosis, in osteoarthritis, 646
- Laminin, as apoptosis protection, 660
- Lansbury systemic manifestations, for rheuma-  
toid arthritis assessment, 740–741
- Larsen method, for rheumatoid arthritis  
radiographic assessment, 729
- Lck kinase, in T-cell receptor signaling, 145
- Leflunomide, for rheumatoid arthritis,  
293–307  
contraindications to, 241  
economic evaluation of, 889  
hepatotoxicity of, 304–306  
mechanism of action of, 293–295  
methotrexate with, 300–304  
pharmacokinetics of, 293  
phase II studies of, 296  
phase III studies of, 296–298  
radiologic evaluation of, 289, 291,  
298–299  
safety of, 239–241  
in pregnancy, 841  
versus methotrexate, 703–704
- Leukemia, musculoskeletal, versus rheumatoid  
arthritis, 279, 281
- Leukocyte(s)  
apoptosis of, in glomerulonephritis,  
664–667  
aspirin-triggered lipoxin effects on, 86  
endothelial cell interactions with,  
99–103  
lipoxin effects on, 79, 81
- Leukocyte-mediated vascular injury, 98–99
- Licofelone, for apoptotic cell clearance, in  
osteoarthritis, 647–648
- LICOS (inducible costimulator molecule), 179,  
182, 186
- “Limited n” studies, in observational  
research, 691
- Linear models, in observational research, 691
- Lipoxygenase inhibitors, for apoptotic cell  
clearance, in osteoarthritis, 647–648
- Lipopolysaccharide, in apoptosis induction,  
577–579
- Lipoxins  
actions of, 68–71  
in cellular systems, 79–81  
in disease, 81–83  
analogs of, 76–77  
aspirin-triggered. See  
Aspirin-triggered lipoxins.  
discovery of, 68  
formation of, 71–75  
in animal models, 77–78  
in human disease, 78  
inactivation of, 75–77  
receptors for, 83–87  
therapies related to, 87–90
- Listeriosis, risk of, in etanercept therapy, 322
- Liver  
autoimmune disease of, interleukin-18 in,  
427–428  
toxicity to, antirheumatic drugs,  
240–241, 251, 304–306
- Longitudinal medical histories, in Rochester  
Epidemiology Project, 823–824
- Lung, inflammation of, lipoxin in, 81–82
- Lupus syndrome, drug-induced, in rheumatoid  
arthritis therapy, 249–251, 340
- Lyme disease vaccine, safety of, 843
- Lymph nodes, apoptotic cell clearance in, 512
- Lymphatic tissue, germinal centers of, apopto-  
tic cell clearance in, 512, 518–521
- Lymphokines, 146
- Lymphoma  
from antirheumatic drug therapy,  
248–249  
adalimumab, 358  
etanercept, 323  
in rheumatoid arthritis, 272–275,  
341–342, 858–859  
musculoskeletal, versus rheumatoid  
arthritis, 279, 281

- Lymphoproliferative disorders, in rheumatoid arthritis, 275–276
- Lysozymes, in phagocytosis, 26–27
- M**
- McGill Pain Questionnaire, for rheumatoid arthritis, 737
- Macrophage(s)
- apoptosis of, resistance to, in rheumatoid arthritis, 609–612
  - HMGBl activation of, 628–629
  - impaired activity of, in systemic lupus erythematosus, 514
  - phagocytic activity of. *See* Phagocytes.
  - tangible body, in systemic lupus erythematosus, 512, 519–520
- Magnetic resonance imaging, in osteoarthritis, 787–788
- Major histocompatibility complex
- autoantigen processing by, dominance and crypticity in, 456–458
  - genes of, in autoimmune disease, 216–224
  - allele association in, 222–224
  - disease classification based on, 221–222
  - importance of, 217–218
  - physiologic response and, 218–220
  - target autoantigen distribution and, 220–221
  - T-lymphocyte repertoire in, 224–227
- Malignancy. *See* Cancer.
- Malononitroamide, as leflunomide metabolite, 293
- Mannose-binding lectin
- gene for, complement deficiencies and, 8–9
  - in apoptotic cell clearance, 479
- Matching, in observational research, 689–690
- Matrix metalloproteinases
- in angiogenesis, 106
  - in rheumatoid arthritis, 45–46
- Mayo Clinic, Rochester Epidemiology Project and. *See* Rochester Epidemiology Project.
- MCH. *See* Major histocompatibility complex.
- Mcl-1 protein, in apoptosis, 449, 603, 611–612
- Medical records, in Rochester Epidemiology Project. *See* Rochester Epidemiology Project.
- Medication Reimbursement Registry, of Scandinavian countries, 855–858, 860–862
- Meloxicam, channeling of, 845
- Membrane cofactor protein
- abnormalities of, in pregnancy, 10
  - action of, 5–6
- Memory T lymphocytes, 149–150
- Mer protein, in apoptosis, 200, 474, 477–478, 532–533
- Mesangial cells, apoptosis of, in glomerulonephritis, 658–661
- Metastasis, arthritis in, versus rheumatoid arthritis, 279–280
- Methotrexate, for rheumatoid arthritis, 704–705, 709, 713
- adalimumab with, 349–350, 352, 355–357, 359
  - anakinra with, 366–367, 369–370
  - apoptosis induction in, 605–606
  - beneficial effects of, 843–844
  - cohort studies of, 695–696
  - cyclosporine with, 704
  - cytotoxic T-lymphocyte antigen 4–immunoglobulin with, 383–385
  - economic evaluation of, 889–890
  - etanercept with, 313–314, 316
  - infliximab with, 332–338
  - interleukin-6 monoclonal antibody with, 410
  - leflunomide with, 300–304
  - malignancy due to, 275
  - safety of, in pregnancy, 841
  - versus etanercept, 314–316, 711
  - versus leflunomide, 296–298, 703–704
- Misoprostol, for osteoarthritis, 705
- Mitochondria-dependent pathway, in apoptosis, 602–603
- Mitogen-activated protein kinase, in phagocytosis, 34–35
- Modified Health Assessment Questionnaire, for rheumatoid arthritis assessment, 729, 735, 737–738
- Molecular mimicry, in tolerance breakdown, 151
- Monoclonal antibodies, to interleukin-6, for rheumatoid arthritis, 408–410
- Monocyte(s), apoptosis of, in glomerulonephritis, 667
- Monocyte chemotactic factor, in apoptosis regulation, 510
- Monocyte-derived dendritic cells
- development and function of, 116–118
  - in rheumatoid arthritis, 123–127

- Mononuclear phagocyte system.  
*See* Phagocytes.
- Mortality  
 in rheumatoid arthritis, 857  
 predictors of, in NHANES, 874
- Multicenter Osteoarthritis Study, 794–795
- Multicentric reticulohistiocytosis, versus  
 rheumatoid arthritis, 276–277
- Multi-Dimensional Health Assessment  
 Questionnaire, for rheumatoid arthritis  
 assessment, 731–733, 735, 737
- Multiple myeloma  
 in rheumatoid arthritis  
 versus rheumatoid arthritis, 279–280
- Multiple sclerosis  
 cytokine inhibitor exacerbation of, 337  
 infliximab exacerbation of, 340–341
- Mycobacterium tuberculosis* infections.  
*See* Tuberculosis.
- Myeloid cells, lipoxin effects on, 79, 81
- Myeloid dendritic cells  
 development and function of, 116–118  
 early control of, 118–119
- Myocardium, apoptosis in, 588–589
- Myofibroblasts, in congenital heart block,  
 596–598
- Myopathies, inflammatory, cytokines in,  
 53–54
- N**
- “n of 1” studies, in observational research, 691
- Nashville, Tennessee, rheumatology databases,  
 772–773
- National Data Bank for Rheumatic Diseases,  
**753–768**  
 data analysis in, 764  
 data collection in  
 methods for, 761–764  
 type of, 755  
 data validation in, 765–766  
 database components in, 754  
 observational data banks versus randomized controlled trials in, 753–754  
 protocols for, 766  
 questionnaire for, 755–761
- National Health and Nutrition Examination  
 Surveys (NHANES), **869–878**  
 musculoskeletal disorder studies in,  
 872–875  
 purpose of, 869
- Survey I, 870  
 Survey II, 870–871  
 Survey III, 871–872
- National Insurance Administration, of  
 Scandinavian countries, 860
- Necrosis  
 description of, 506–507  
 HMGB1 release in, 509, 629–630  
 in osteoarthritis, 644  
 in systemic lupus erythematosus, 574  
 cell clearance in, 494–496  
 T-lymphocyte tolerance and, 515  
 regulation of, 667  
 versus apoptosis, 506–507, 638
- Neonatal lupus syndrome, heart block in. *See*  
 Congenital heart block.
- Neovascularization  
 endothelium role in  
 clinical perspectives of, 107–108  
 pathophysiology of, 104–107  
 in rheumatoid arthritis, 44–45  
 inhibitors of, 106–107
- Neutrophil(s)  
 apoptosis of  
 in glomerulonephritis, 664–667  
 in inflammation resolution,  
 604–605  
 in rheumatoid arthritis, 612  
 HMGB1 activation of, 628–629  
 phagocytic activity of. *See* Phagocytes.
- NHANES. *See* National Health and Nutrition  
 Examination Surveys (NHANES).
- Nitric oxide  
 in apoptosis, 642–643, 661  
 in phagocytosis, 27
- Nitric oxide synthase inhibitors, for apoptotic  
 cell clearance, in osteoarthritis, 647
- Nonsteroidal anti-inflammatory drugs  
 authorization for, 845  
 economic evaluation of, 888–889  
 for osteoarthritis, 648  
 for rheumatoid arthritis, 713–714  
 lipoxin activation by, 76  
 prospective cohort studies on, 805–807  
 safety of, 839–840  
 in pregnancy, 842
- Nordic Biological Specimen Banks for Cancer  
 Causes and Control, 856–857
- Normative Aging Study, 801, 810–811
- NSAIDs. *See* Nonsteroidal  
 anti-inflammatory drugs.
- Nuclear factor KB, in apoptosis  
 in osteoarthritis, 643–644  
 in rheumatoid arthritis, 610–612, 614

Nucleosomes, in systemic lupus erythematosus, 494–495, 527–555  
antibodies to, 537–546  
antigenicity of, factors contributing to, 535–536  
balance of, 529–531  
cell clearance defects and, 531–533  
modification of, 533–535  
sources of, 527–528  
structure of, 529  
T-lymphocyte recognition of, 536–537

Nurses Health Study, 800, 802–805

## O

Observational research, 685–699  
causal inference in, 686–691  
causal (structural) models in, 691  
causal research and, 688–689  
causation in, 686–687  
comparability in, 686–687, 689–690  
conventional methods in, 689–690  
conventional modeling in, 690–691  
data banks for  
data analysis in, 764  
data collection in, 755, 761–764  
data validation in, 765–766  
database components in, 754  
protocols for, 766  
questionnaire for, 755–761  
versus randomized controlled trials, 753–754  
descriptive, 685–686  
for diagnostic studies, 696  
future of, 696–697  
inverse probability of treatment  
weighting methods in, 690  
randomized trials in, 687–688  
types of, 691–696

Ocular pressure, lipoxin effects on, 83

Olmstead County, Minnesota, Rochester Epidemiology Project and. *See* Rochester Epidemiology Project.

Oslo Rheumatoid Arthritis Registry, 773–774

Osteoarthritis  
apoptosis in, 637–651  
cell biology and, 648–649  
cell senescence and degeneration in, 646–647  
cellular features of, 637–640  
incidence of, 639, 641  
inductive mechanism of, 641–644  
morphology of, 644–646  
therapeutic options related to, 647–648  
cytokines in, 47

epidemiology of, 783–797  
current insights into, 783–784  
current studies of, limitations of, 784–789  
Multicenter Osteoarthritis Study of, 794–795  
Osteoarthritis Initiative study of, 794–795  
study design parameters for, 789–794  
in NHANES, 872–873  
medical record data on, in Rochester Epidemiology Project, 821, 830  
onset of, 789–792  
progression of, 788–789  
prospective cohort studies on, 800–801, 804–805, 811–813  
risk factors for, 784–786, 788–792  
treatment of, clinical trials of, 705–706

Osteoarthritis Initiative study, 794–795

Osteoclasts, apoptosis of, in rheumatoid arthritis, 616–617

Osteoporosis, in NHANES, 874–875

Osteoprotegerin ligand, in rheumatoid arthritis, 149

Outcomes. *See also* Health services research.  
long-term, in Rochester Epidemiology Project, 824–825  
questionnaires for, 755–761

OX40, in T-lymphocyte afferent signal regulation, 179

## P

p53 gene product, in apoptosis, in rheumatoid arthritis, 616

PACES (Patient Preference for Placebo, Acetaminophen or Celecoxib Evaluation Studies), 705–706

Pain  
in osteoarthritis, threshold of, 792–794  
in rheumatoid arthritis, assessment of, 736–737

Palmar fasciitis, versus rheumatoid arthritis, 276, 278

Pancytopenia, from cytokine inhibitors, for rheumatoid arthritis, 247

Panniculitis, versus rheumatoid arthritis, 276, 278

Parallel design, for rheumatoid arthritis clinical trials, 702–704

Parametric methods, in observational research, 690–691

- Paraneoplastic syndromes, versus rheumatoid arthritis, 276–279
- Paraprotein, in osteoarthritis, 639
- Paroxysmal nocturnal hemoglobinuria, complement deficiency in, 9–10
- Pathogen-associated molecular patterns (PAMPs), 142–143, 493–494
- Pathology specimens, in Rochester Epidemiology Project, 824
- Patient only index, for rheumatoid arthritis assessment, 742–744
- Patient Preference for Placebo, Acetaminophen or Celecoxib Evaluation Studies (PACES), 705–706
- Pattern recognition molecules, in phagocytosis, 594
- Pattern-recognition receptors, 142–143
- Paulus criteria, for rheumatoid arthritis assessment, 741–742
- PD-1, in T-lymphocyte afferent signal regulation, 180, 185, 187
- Permethis vulgaris, HLAs in, 224
- Penetrance rate, of autoimmune disease, 215–216
- Penicillamine, for rheumatoid arthritis, 709, 713
- Pentraxin PTX3, in apoptosis regulation, 511
- Perforin, in cytotoxic T lymphocytes, 148
- Peripheral tolerance, in apoptosis, 203–204
- Phagocytes, 19–38
- action of, definition of, 23
  - apoptotic cell recognition by, 199–200
  - during transition from acute to chronic inflammation, 22–25
  - dysregulation of, 29–34
    - macrophage activation, 30–31
    - neutrophil activation, 29–30
  - mediators produced by, 25–29, 34–35
  - migration mechanisms of, 20–22
  - receptor interactions with, 23–24
- Phagocytosis, in apoptosis. *See also* Apoptosis, clearance in.
- chemoattractants in, 509–511
  - defective, 668–669
  - in congenital heart block, 594–598
  - in different tissues, 511–513
  - in kidney, 654–655
  - signals in, 488–491, 507–508
- Pharmacoepidemiology, 835–850
- confounding and bias in, 837–838
  - data sources for, 836–837
- drug beneficial effect studies in, 843–845
- drug safety studies in, 838–843
- alendronate, 842–843
  - cyclooxygenase-2 inhibitors, 840–841
  - in pregnancy, 841–842
  - Lyme disease vaccine, 843
  - NSAIDs, 839–840
  - tumor necrosis factor- $\alpha$  inhibitors, 843
- study designs for, 837
- Phosphatase and tensin homolog deleted from chromosome 10 (PTEN), in apoptosis, in rheumatoid arthritis, 614
- Phosphatidylserine, in apoptosis in cell clearance, 476–477
- recognition of, 199–200
- Phospholipase, secretory, in apoptosis regulation, 510–511
- Phospholipids, in apoptotic cell clearance, 508
- Phosphorylation, of autoantigens, in apoptosis, 465
- Physical activity, in NHANES, 874
- Physical examination, for rheumatoid arthritis assessment, 726
- PI3K/Akt-1 pathway, in apoptosis, in rheumatoid arthritis, 611, 614
- Plasmacytoid dendritic cells, development and function of, 119–120
- Polyarthritis
- carcinomatous, versus rheumatoid arthritis, 276–277
  - inflammatory, disease-modifying anti-rheumatic drug therapy for, 694
- Polymyalgia rheumatica, medical record data on, in Rochester Epidemiology Project, 821, 825, 830
- Polymyositis, cytokines in, 53–54
- Polyomavirus infections, autoimmunity in, 536
- Population Registry, of Scandinavian countries, 853–854, 857–858, 861
- Poxvirus apoptosis inhibitory protein, 444
- Prednisolone, for rheumatoid arthritis, 704
- Pregnancy
- complement regulation in, 10
  - drug safety in, 841–842
  - rheumatoid arthritis therapy in
    - adalimumab, 359
    - cytokine inhibitors, 251–252
    - leflunomide, 241
- SLE in, congenital heart block in. *See* Congenital heart block.

- Prescription Registry, of Scandinavian countries, 855–856, 860
- Programmed cell death 1 protein, in T-lymphocyte afferent signal regulation, 179–180
- Propensity score methods, in observational research, 690
- Prospective cohort studies, 799–817  
both male and female, 801, 811–814  
causal inferences from, 692–696  
characteristics of, 799–802  
female, 800, 802–808  
infrastructure for, in Rochester Epidemiology Project, 826–827  
male, 801, 808–811  
of drugs, 837
- Prostaglandins  
in angiogenesis, 106  
in phagocytosis, 29
- Proteolysis, novel or impaired, in apoptosis, autoimmunity induction in, 458–459
- P-selectin glycoprotein ligand 1, in phagocytosis, 21
- Psoriatic arthritis  
cytokines in, 46  
etanercept for, 318–320  
familial aggregation of, 213–214  
medical record data on, in Rochester Epidemiology Project, 821, 825, 830
- P2X-7 receptor, in interleukin-18 secretion, 418–419
- Q**
- Questionnaires  
for outcomes research, 755–762  
comprehensive versus brief, 755–757  
data capture in, 759, 761  
duplication of content in, 757–758  
Internet-based, 759, 761–762  
problems with, 759  
treatment data in, 759–760  
for rheumatoid arthritis assessment, 726, 730–736, 739–740, 744–746
- R**
- Rac2 protein, in apoptotic cell clearance, 474
- Radiology  
in osteoarthritis epidemiologic studies, 786–788  
in rheumatoid arthritis assessment, 726, 728–729, 738–739
- in rheumatoid arthritis treatment evaluation, 285–292  
anakinra, 289, 372–373  
data analysis and presentation in, 287–288  
etanercept, 289–290, 315–316  
infliximab, 289–291  
leflunomide, 289, 291, 298–299  
scoring issues in, 286–287  
study design for, 285–286  
records of, in Rochester Epidemiology Project, 824
- Randomized controlled trials  
in causal research, 687–688  
versus observational data banks, 753–754
- RANK and RANKL, in apoptosis, in rheumatoid arthritis, 616–617
- Ratingen score, for rheumatoid arthritis radiographic assessment, 729
- Raynaud's phenomenon, apoptosis dysregulation in, 197
- Reactive arthritis, cytokines in, 46
- Reactive nitrogen species, in phagocytosis, 27
- Reactive oxygen species, in phagocytosis, 27
- Recall bias, minimization of, in Rochester Epidemiology Project, 828–829
- Receptor for advanced glycation end-products, HMGB1 interactions with, 628–629
- Referral bias, minimization of, in Rochester Epidemiology Project, 827
- Registry of Population Changes, of Scandinavian countries, 858
- Regression models, in observational research, 691
- Regulators of complement activity, 5–6
- Remitting seronegative symmetric synovitis with pitting edema, versus rheumatoid arthritis, 276–277
- Research, observational. *See* Observational research.
- Resoleomics, in inflammation. *See* Inflammation, resolution of, endogenous small molecules for.
- Resolvins, in inflammation, 90–91
- Reticulohistiocytosis, multicentric, versus rheumatoid arthritis, 276–277
- Rheumatism, postchemotherapy, versus rheumatoid arthritis, 276, 278–279

- Rheumatoid arthritis  
 apoptosis in, **601–623**  
     current therapy based on, 605–607  
     death-receptor pathway in, 601  
     inflammation resolution, 604–605  
     incidence of, 603–604  
     mitochondria-dependent pathway in, 602–603  
     resistance to  
         in fibroblasts, 612–616  
         in macrophages, 609–612  
         in neutrophils, 612  
         in osteoclasts, 616–617  
         in T lymphocytes, 607–609  
     therapy based on, 607–617
- B lymphocytes in, 168–169  
 cancer incidence in, 858–859  
 clinical trials and clinical care in, **701–724, 725–751**  
 designs of, 702–706  
     cross-over, 705–706  
     influencing results, 715  
     parallel, 702–704  
     step-down, 704–705  
     step-up, 704  
 limitations of, 706–717  
     intrinsic, 715–717  
     pragmatic, 709–715  
 long-term observational research for, 717–718  
 quantitative measures and  
     indices for  
     advantages and disadvantages of, 738–740  
 American College of Rheumatology data set, 741–743  
 disease activity score, 742–743  
 fatigue measurement, 737  
 functional, 726, 738–739  
 global, 726, 738–739  
 joint counts, 726–728, 739  
 laboratory tests, 726, 729–730, 739  
 Lansbury systemic manifestations, 740–741  
 pain measurement, 736–737  
 patient only index, 742–744  
 Paulus criteria, 741–742  
 physical examination, 726  
 questionnaires, 726,  
     730–736, 739–740,  
     744–746  
 radiography, 726, 728–729,  
     738–739  
 simplified disease activity index, 742–743  
 standard protocol for, 744, 746  
 Steinbrocker therapeutic scorecard, 740–741  
 complement in, 12–13  
 cytokines in, 40–46  
 databases for, **769–781**  
     American Rheumatism Association Medical Information System, 770–771  
     Central Finland Rheumatoid Arthritis Database, 775  
     German Regional Collaborative Arthritis Centers, 774–775  
     Italian, 777  
     Nashville, Tennessee, 772–773  
     Oslo Rheumatoid Arthritis Registry, 773–774  
     Spanish, 776–777  
     Standard Diagnosis Registry of Rheumatic Diseases, 773  
     Swedish registry of biologic agents and leflunomide, 776  
     uniform, 777  
     Wichita Database and National Data Bank, 771–772  
 familial aggregation of, 214  
 genetic factors in, 215, 859–860  
 HLAs in, 223–224  
 juvenile. *See Juvenile chronic arthritis*/  
     juvenile rheumatoid arthritis.  
 malignancy and. *See Cancer*.  
 medical record data on, in Rochester Epidemiology Project, 821–831  
 monocyte-derived dendritic cells in, 123–127  
 mortality in, 857  
 pathogenesis of, 363–364  
     interleukin-6 in, 406–407  
     interleukin-18 in, 415–432  
 population studies of, 861–862  
 prospective cohort studies on, 800, 804, 806  
 T lymphocytes in, 149  
 treatment of. *See also specific drugs*.  
     adalimumab in. *See Adalimumab*.  
     anakinra in. *See Anakinra*.  
     angiogenesis inhibitors in, 108  
     assessment of  
         quantitative measures and indices for, **725–751**  
         radiology in, **285–292**  
     B-lymphocyte considerations in, 170, 391–401  
     clinical trials and care in. *See*  
         Rheumatoid arthritis, clinical trials and clinical care in.  
     costimulatory molecules in, 186  
     cytotoxic T-lymphocyte antigen 4-immunoglobulin in, 379–389

- databases on, 741–743,  
**769–781**, 860
- etanercept in. *See* Etanercept.
- high-mobility group box  
chromosomal protein 1  
(HMGB1) inhibitors in,  
**625–635**
- infliximab in. *See* Infliximab.
- interleukin-6 inhibitors in,  
**403–413**
- interleukin-18 inhibitors in,  
**415–422**
- leflunomide in. *See* Leflunomide.
- malignancy due to, 274–276
- methotrexate in. *See* Methotrexate.
- radiologic efficacy of. *See*  
Radiology, in rheumatoid  
arthritis treatment evaluation.
- safety of, **237–255**. *See also*  
Tuberculosis, risk of, from  
rheumatoid arthritis therapy.
- adalimumab, 242–252,  
356–359
- anakinra, 242–252, 369–372
- cytokine inhibitors, 242–252
- infliximab, 242–252,  
339–342
- leflunomide, 239–241
- twin concordance in, 215
- Rheumatoid factor
- cells producing, activation of, chromatin-containing immune complexes in,  
560–564
- in rheumatoid arthritis assessment, 730
- Rituximab, for rheumatoid arthritis, **391–401**
- aim of, 391–393
- immunodynamic studies of, 399–400
- immunosuppression evidence in,  
396–397
- indications for, 398
- infusion reactions from, 397–398
- justification for, 396
- length of benefit of, 396
- malignancy due to, 398
- mechanics of, 393–394
- practical experience with, 394
- protocols for, 394–395
- seronegative, resistance of, 395
- Rochester Epidemiology Project, **819–834**
- bias minimization in, 827–829
- conditions inadequately captured in  
health care system in, 825
- contemporary diagnostic criteria applied  
in, 822
- cost-of-illness studies in, 830
- costs of, 830
- delayed effects in, 824–825
- encounter-specific data in, 821
- genetic, 825–826
- history of, 819–821
- indexing system of, 820
- information on confounding factors  
in, 826
- infrastructure for prospective studies  
in, 826–827
- longitudinal medical histories in,  
823–824
- long-term outcomes in, 824–825
- original medical record access in, 821
- reassessment of original slides,  
radiographs, and specimens in, 824
- representativeness of county population  
in, 829–830
- secular trend analysis in, 822–823
- subject protection in, 831
- unique study designs and analysis in,  
830–831
- Rofecoxib, safety of, 840–841
- 
- S
- S19 ribosomal protein dimer, in apoptosis regulation, 510
- Safety, drug
- in rheumatoid arthritis. *See* Rheumatoid arthritis, treatment of, safety of.
- pharmacopidemiologic studies of,  
838–843
- Scleroderma autoantigen (CENP-C), cleavage of, in apoptosis, 463
- Secular trends, analysis of, in Rochester Epidemiology Project, 822–823
- Selectins
- in angiogenesis, 106
- in leukocyte–endothelial interactions,  
100–101
- in phagocytosis, 20–21
- Senescence, of T lymphocytes, 153–154
- Sentrin-1/SUMO-1, in apoptosis, in rheumatoid arthritis, 615
- Sepsis, high-mobility group box chromosomal protein 1 (HMGB1) in, 627–628
- SF-36 questionnaire, for rheumatoid arthritis assessment, 730
- Sharp method, for rheumatoid arthritis radiographic assessment, 728–729
- Silicone breast implants, rheumatic disease in, prospective cohort studies on, 803–804
- Simplified disease activity index, for rheumatoid arthritis assessment,  
742–743

- Sjögren's syndrome, medical record data on, in Rochester Epidemiology Project, 821, 830
- Skin, inflammation of, lipoxin in, 81
- SLE. *See* Systemic lupus erythematosus.
- Soluble interleukin-18 receptor, 423–424
- SPERA (standard protocol to evaluate rheumatoid arthritis), 744, 746
- Spondyloarthropathies
- cytokines in, 46
  - family aggregation of, 213–214
  - HLA-B27 in, 222
- SSA/Ro autoantibodies, in congenital heart block. *See* Congenital heart block.
- SSB/La autoantibodies, in congenital heart block. *See* Congenital heart block.
- Standard Diagnosis Registry of Rheumatic Diseases, 773
- Standard gamble technique, in health services instruments, 884–885
- Standardization, in observational research, 689
- STAT3, in apoptosis, in rheumatoid arthritis, 614–615
- Statins, beneficial effects of, 844
- Steinbrocker therapeutic scorecard, for rheumatoid arthritis assessment, 740–741
- Step-down design, for rheumatoid arthritis clinical trials, 704–705
- Step-up design, for rheumatoid arthritis clinical trials, 704
- Still's disease, cytokines in, 46–47
- Stratification, in observational research, 689
- Stromal cell-derived factor 1, in rheumatoid arthritis, 607
- Sulfasalazine
- for rheumatoid arthritis, 606, 703–705, 709
  - safety of, in pregnancy, 841
- SUMO-1, in apoptosis, in rheumatoid arthritis, 615
- Surfactant proteins, in apoptotic cell clearance, 479
- Surveillance bias, minimization of, in Rochester Epidemiology Project, 828
- Survival bias, minimization of, in Rochester Epidemiology Project, 827–828
- Swedish registry of biologic agents and leflunomide, 776
- Synoviolin/Hrd1, in apoptosis, in rheumatoid arthritis, 615
- Synovitis
- chronic, 44
  - initiation of, 40–41
  - perpetuation of, 41–44
  - remitting seronegative symmetric, with pitting edema, versus rheumatoid arthritis, 276–277
- Systemic lupus erythematosus
- apoptosis in, 505–526, 527–555
    - abnormal cell clearance in, 493–499
    - animal models of, 513–514
    - antigen formation in, 494–495, 527–528, 533–536
    - B lymphocytes and, 516–517, 519–521
    - balance of, 528–531
    - cell clearance and, 481–482, 494–499, 531–533
    - DNA release in, 573–585
    - genetic factors in, 517–518
    - germinal centers and, 512, 518–521
    - in kidney, 668
    - mechanisms of, 507–511
    - nephritis and, 543–546
    - nucleosome-specific antibodies in, 537–546
    - phagocytosis in, 507–513
    - rate of, 514
    - secondary necrotic cell accumulation in, 515
    - T lymphocytes and, 514–515, 536–537
    - versus necrosis, 506–507
    - versus normal clearance mechanisms, 488–494
  - B lymphocyte function in, 168–169
  - complement deficiencies in, 7–9
  - cytokines in, 47–52
  - dendritic cell cross-priming in, 125–126
  - family aggregation of, 213–215
  - immune complexes in, Toll-like receptor interactions with, 564
  - in pregnancy, congenital heart block in. *See* Congenital heart block.
  - medical record data on, in Rochester Epidemiology Project, 821, 825, 830
  - necrosis in, cell clearance in, 494–496
  - prospective cohort studies on, 800, 804, 807

- treatment of  
 B lymphocyte considerations  
 in, 168  
 complement-related, 11–12  
 costimulatory molecules in, 186
- Systemic sclerosis  
 cytokines in, 52–53  
 versus number of children, 861
- Systemic vasculitis, farming exposure and, 693
- T**
- T lymphocytes, 135–157  
 activation of, 143–146  
 apoptosis of, resistance to, in rheumatoid arthritis, 607–609  
 autoimmunity and, 150–153, 224–227, 458–460  
 costimulatory molecule interactions with.  
*See* Costimulatory molecules.  
 cytotoxic, 148–149  
 antigen 4–immunoglobulin, for  
 rheumatoid arthritis, 379–389  
 in apoptosis, 661  
 in autoantigen structural alterations, 461–464  
 development of, 139–141  
 helper, 146–148  
 in antigen recognition, 136–138  
 in rheumatoid arthritis, 41–44  
 in systemic lupus erythematosus, 51, 516, 536–537  
 in tuberculosis, 259–260  
 innate immunity and, 141–143  
 lineage commitment of, 139–141  
 memory, 149–150  
 receptors for. *See* T-cell receptor.  
 regulation of, 143–146  
 regulatory, 152  
 self-recognition by, 219  
 senescence of, 153–154  
 subsets of, autoimmune disease and, 224–227  
 suppressor, 152  
 tolerance and, 150–153, 514–515  
 types of, 135–136
- T-cell receptor  
 diversity of, 138  
 function of, 136–138  
 self-recognition by, 219  
 structure of, 138
- Teratogens, 841–842
- Terminal deoxynucleotidyl transferase-mediated dUTP-biotin nick end-labeling (TUNEL), in apoptosis detection, 657–658  
 in congenital heart block, 592  
 in rheumatoid arthritis, 603–604
- Thrombocytopenia, immune, rituximab for, 398
- Thrombospondin-1, in apoptosis, in congenital heart block, 595
- Thymus, apoptotic cell clearance in, 512
- Time trade off technique, in health services instruments, 884–885
- TNFR (tumor necrosis factor- $\alpha$  receptor, in apoptosis, in rheumatoid arthritis), 610–611
- TNFR1-associated DD protein (TRADD), in apoptosis, in rheumatoid arthritis, 610
- TNFR-associated factors (TRAFs), in apoptosis, in rheumatoid arthritis, 610
- Tolerance  
 B lymphocytes in, 162–164  
 induction of, in apoptosis, 456  
 peripheral, in apoptosis, 203–204  
 T-lymphocyte dependent, 150–153
- Tolerogenic dendritic cells, 123–124
- Toll-like receptors  
 HMGB1 interactions with, 628  
 in immune regulation, 493–494  
 in phagocytosis, 31  
 nuclear antigen stimulation of, 557–572  
 AM14B cells, 562–563  
 apoptosis and, 564–567  
 autoantigens in, 557–558  
 bacterial DNA, 558  
 dsDNA fragments, 563–564  
 immune complexes and, 560–562, 564  
 in lupus sera, 564  
 ligands recognized by, 558–559  
 rheumatoid factor-producing B cells and, 559–562  
 therapeutic agents based on, 567  
 of dendritic cells, 121  
 T lymphocyte function and, 142–143
- TRADD (TNFR1-associated DD protein), in apoptosis, in rheumatoid arthritis, 610
- TRAFs (TNFR-associated factors), in apoptosis, in rheumatoid arthritis, 610
- TRAIL and TRAIL receptors, in apoptosis, in rheumatoid arthritis, 608–609, 613–614
- TRANCE, in rheumatoid arthritis, 149
- Transforming growth factor- $\beta$   
 in apoptosis, 478, 595–596  
 in inflammatory myopathies, 54  
 in systemic sclerosis, 52–53
- Transglutaminase 2, in apoptotic cell clearance, 478

- Transglutamination, in apoptosis, in autoantigen structural alterations, 466
- Tuberculosis, risk of, from rheumatoid arthritis therapy, 257–270  
adalimumab, 357–359  
anakinra, 267  
cytokine inhibitors, 245–247  
epidemiology and, 257–258  
etanercept, 322  
immune defense and, 258–260  
infliximab, 339–340  
screening in, 263, 265–266  
treatment of positive cases, 266–267  
tumor necrosis factor inhibitors, 260–263
- Tumor necrosis factor and tumor necrosis factor receptor family, 176, 182–184  
etanercept as. *See* Etanercept.  
inhibitors of  
    infliximab as. *See* Infliximab.  
    safety of, 843  
    tuberculosis risk from, 260–263
- Tumor necrosis factor- $\alpha$   
    antibodies to, for rheumatoid arthritis, 606–607, 625–626  
    in apoptosis, 660–661  
        in clearance, 477–478  
        in osteoarthritis, 643–644  
        in rheumatoid arthritis, 610–612, 614  
    in dendritic cell development, 118–119  
    in inflammatory myopathies, 53–54  
    in phagocytosis, 31–35  
    in rheumatoid arthritis, 41–45  
    in systemic lupus erythematosus, 47–52
- Tumor necrosis factor- $\alpha$  receptor, in apoptosis, in rheumatoid arthritis, 610–611
- Tumor necrosis factor-related apoptosis-inducing ligand, in systemic lupus erythematosus, 49
- Twin concordance, in autoimmune disease, 215

**U**

- Uric acid, in apoptosis regulation, 510

**V**

- Vaccine, Lyme disease, safety of, 843
- van der Heijde modification, of Sharp score, for rheumatoid arthritis radiographic assessment, 729
- Vascular cell adhesion molecule-1, in leukocyte-endothelial interactions, 101
- Vascular endothelial cells. *See* Endothelial cells, vascular.
- Vascular endothelial growth factor  
    glomerulonephritis and, 662–663,  
        669–670  
    in angiogenesis, 104
- Vasculitis  
    cytokines in, 54–56  
    systemic, farming exposure and, 693
- Vasodilatation, in inflammation, 98–99
- Viral infections, autoimmunity in, 535–536
- Visual analog scale  
    for rheumatoid arthritis, 737  
    in health services instruments, 884–885
- Volunteer bias, minimization of, in Rochester Epidemiology Project, 828

**W**

- Walk time, in rheumatoid arthritis assessment, 738
- Wegener's granulomatosis  
    cytokines in, 55–56  
    etanercept for, 321
- Western Ontario and McMaster Universities arthritis index, for rheumatoid arthritis assessment, 730, 737
- Wichita Database and National Data Bank, 771–772
- Wiskott-Aldrich protein, in apoptotic cell clearance, 474
- Women's Health Study, 800, 807–808

**Z**

- ZAP-70, in apoptosis, in rheumatoid arthritis, 609



